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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,637	04/27/2001	Anthony Robert Milnes Coates	Q-64007	9237

7590 05/26/2004

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EXAMINER	
MARX, IRENE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,637	COATES ET AL.	
	Examiner	Art Unit	
	Irene Marx	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,9 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7 and 9-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendment filed 4/9/04 is acknowledged. Claims 2-7 and 9-10 are being considered on the merits

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-7 and 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is vague and indefinite in the recitation of "an antibiotic which is capable of killing growing bacteria" since it is not clearly set forth under which circumstances the antibiotic will or will not carry out the function of killing bacteria.

Claim 9 is vague, indefinite and inconsistent in the recitation at step (a) of growing an antibiotic-sensitive strain to stationary phase to **thereby obtain** a dormant culture". Generally, the term dormant is understood to mean "not growing". Yet, in stationary phase not all bacteria are "dormant" (not growing), but rather there is slowing down of the growth rate. Moreover, in subsequent step (b) the allegedly "dormant" (not growing) culture is treated with an antibiotic to kill growing bacteria and to obtain a "phenotypically antibiotic-resistant subpopulation". As the cells are indicated to be dormant, all of the cells are incapable of growth and are impervious to an antibiotic that kills growing cells regardless of their "sensitivity" thereto. In other words, the claim is inconsistent and contradictory, inasmuch as a dormant culture is treated wherein no bacteria would be growing and the antibiotic capable of killing growing cells would be ineffective to kill any cells. In addition, the process as claimed is confusing because is no clear claim designated indication that "antibiotic-sensitive" and "antibiotic-resistant" pertain to one and the same antibiotic. Thus, claim 9 is inconsistent, contradictory and confusing requiring killing "growing bacteria" which are, in fact, simultaneously indicated to be "dormant". Thus, the material isolated in the step of "isolating a phenotypically antibiotic-resistant subpopulation" cannot be properly ascertained. The claim is also indefinite in that "selected pharmaceutically acceptable concentration" is not clearly defined in the specification. Therefore, the amount intended cannot be readily ascertained. Is it an amount for *in vitro* or *in vivo* treatment and for

which compound to treat which bacteria? How is this amount to be determined? How is the "pharmaceutically acceptable concentration" selected?

Claim 9 is vague and indefinite in that the antecedent basis for "said dormant bacteria" in item (iii) is uncertain. It is noted that "a dormant culture" is obtained in step (a) prior to treatment with an antibiotic which is capable of killing growing bacteria.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-4, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Entenza *et al.* I (1996) or Entenza et al. *II (1994)* for the reasons as stated in the last Office action and the further reasons below.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Applicant argues that Entenza *et al.* (II) is not directed to identification of drugs capable of killing dormant bacteria that are already resistant to an antibiotic. However, the claimed invention is not directed to identification of drugs capable of killing dormant bacteria that are already resistant to an antibiotic. As noted previously, claim 9 is directed to (a) of growing an antibiotic-sensitive strain to stationary phase to **thereby obtain** a dormant culture", wherein no resistance is apparent. Since the culture is dormant, no bacteria would be growing and the antibiotic capable of killing growing cells would be ineffective. See also the rejection under 35 U.S.C § 112, second paragraph.

Given that no resistance is induced by the "first" antibiotic and streptomycin is admittedly present in the medium, the subsequent use of penicillin can reasonably deemed to constitute the test compound. The phrase "the streptomycin does not kill growing bacteria of the same strain as the dormant bacteria" is not understood. The claim as written appears to require dormant bacteria to grow, which is incorrect.

Whether or not streptomycin kills growing bacteria of the same strain as the dormant bacteria is irrelevant to the as-claimed invention. All that is required is an antibiotic "which is capable of killing growing bacteria of the same strain".

Therefore the rejection is deemed proper and it is adhered to.

Claims 3-4, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Boswell *et al.* for the reasons as stated in the last Office action and the further reasons below.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Applicant argues that Boswell *et al.* (II) is not directed to identification of drugs capable of killing dormant bacteria that are already resistant to an antibiotic. However, the claimed invention is not directed to identification of drugs capable of killing dormant bacteria that are already resistant to an antibiotic. As noted previously, claim 9 is directed to (a) of growing an antibiotic-sensitive strain to stationary phase to **thereby obtain** a dormant culture", wherein no resistance is apparent. Since the culture is dormant, no bacteria would be growing and the antibiotic capable of killing growing cells would be ineffective. See also the rejection under 35 U.S.C § 112, second paragraph.

It is noted that the strains obtained by Boswell are resistant to macrolide, lincosamide and streptogramin B type antibiotics (page 29, col. 1, paragraph 2). Therefore, the argument that the antibiotic and the test compound are not distinct is incorrect. Even though the reference does not specifically test dormant cells for resistance to macrolide, lincosamide and streptogramin B type antibiotics, it can reasonably be presumed that such resistance is inherent in the strains. It is the Examiner's position that the functional limitations recited are not sufficient to patentably distinguish over the reference. There is a clear inconsistency between dormant cells which are also growing cells as claim designated.

Therefore the rejection is deemed proper and it is adhered to.

Claims 3-4, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Tuomanen *et al.* for the reasons as stated in the last Office action and the further reasons below.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Applicant argues that Toumanen does not describe both steps a) and b) of (i). However, careful reading of page 103, paragraphs 2 and 3, shows that cells were grown in penicillin to treat nongrowing cells and that the test compound was pneumococcal autolysin.

Therefore the rejection is deemed proper and it is adhered to.

Claims 2-4, 6-7 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Entenza *et al.* I (1996*)* or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* taken with Shomura *et al.* and Barth for the reasons as stated in the last Office action and the further reasons below.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Entenza *et al.* I (1996*)* or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* taken with Shomura *et al.* and Barth taken with Shomura *et al.* and Barth as applied to claims 2-4, 6-7 and 9-10 above, and further in view of Murray *et al.* and *The Merck Index* for the reasons as stated in the last Office action and the further reasons below.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

The arguments regarding Entenza *et al.* I (1996*)* or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* are addressed *supra.*

With respect to Shomura, the fact that the use in the reference is merely "growth inhibitory" is noted. However, that does not mean that the dosage cannot be increased such that it is sufficient to kill growing bacteria. It is well recognized in this art to adjust dosage according to need and the claim does not specify a particular amount to be used. Moreover, there is no claim designated proviso to kill **all** growing cells as implied by the argument.

With regard to the timing of "amplification", applicant's reasoning is noted. However, the rejection made is not an anticipation rejection and it is submitted that it would have been obvious to one of ordinary skill in the art to carry out amplification at a convenient time. Moreover, the significance now attributed to this particular step is not clear, even when reading the claim in light of the specification. Therefore, it is not apparent that timing of "amplification" of a compound, which may be an old and well known compound, would provide a patentable distinction over the reference as argued.

In response to applicant's arguments that Barth does not teach dormant bacteria, it is noted that this reference is relied principally upon for its disclosure of ampicillin resistant *S. aureus*.

As to the argument that a skilled person would not seek to combine Murray with the other references because the teachings in Murray are in a different technical field, genetic as opposed to phenotypic resistance, it is noted that the method of making a phenotypically antibiotic-resistance subpopulation has not been shown with objective evidence to provide a subpopulation which has "phenotypic resistance" as argued. In any event, Murray was relied upon to demonstrate that resistance to rifampicin is known, regardless of the mechanisms involved.

Applicant's arguments are not persuasive of error in the rejection. Therefore, the rejection is maintained.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (571) 272-0919. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Irene Marx
Primary Examiner
Art Unit 1651